ARE THE SUPERIOR CERVICAL GANLIA INDISPENSABLE TO THE MAINTENANCE OF LIFE?

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Read before the Academy, April 26, 1920

The sympathetic nerve fibres which originate in the thoracic part of the spinal cord terminate in the superior cervical ganglia, from which separate bundles of nerve fibres go to the various parts of the head. Experiments with stimulation of the central end of the cervical sympathetic nerves revealed that these nerve fibres control various functions localized in the head. For instance, to mention the more important ones, the contraction and dilatation of the bloodvessels of various parts of the head, the constriction and dilatation of the iris and the secretion of various glands. Section of the sympathetic nerve showed that some of these innervations are in a state of tonus, for instance, the pupils become constricted and the bloodvessels of the ear (to be seen best in rabbits) become dilated. By means of local application of nicotine to the ganglia which paralyzes postganglionic but does not affect preganglionic nerve fibres, Langley has shown that some of the postganglionic nerve fibres of the superior cervical ganglia are simply a continuation of the cervical sympathetic, preganglionic nerve fibres, while other postganglionic nerve fibres have their origin in nerve cells within the superior cervical ganglia.

About sixteen years ago we[1] showed that epinephrin (adrenalin) which, if administered by subcutaneous injection, or by instillation in the conjunctival sac, in normal animals, shows no influence upon the size of the pupil, produces promptly a dilatation of the pupil and a considerable reduction of its responsiveness to light, if the subcutaneous injection or the instillation were made in animals in which the corresponding ganglion was removed. To obtain this result the subcutaneous injection or instillation must be made about twenty-four hours in rabbits and forty-eight hours in cats and dogs after the removal of the ganglion. Cutting of the cervical sympathetic nerves has no such effect. These facts were best illustrated in an experiment in which the superior cervical ganglion was removed on one side and the sympathetic nerve was cut on the other side. A simultaneous instillation of adrenalin in both conjunctival sacs caused a dilatation of the pupil on the side in which the ganglion was removed, but not on the side in which merely the sympathetic nerve was cut. For that reason we designated this pupilary phenomenon as "paradoxical." These experiments revealed that in the normal state, and for twenty-four hours in rabbits, or for forty-eight hours in cats and dogs, after the removal of the superior cervical ganglion, the normal condition of the pupil is maintained by influences which take their origin in nerve cells within the superior cervical ganglion and not in the spinal cord.

In studying at various times certain phases of this experiment, I was sometimes annoyed by failures which were caused by early deaths of the animals. A survey of these failures revealed the fact that they took place in animals in which both ganglia were removed. A survey of the several changes in the functions which stimulation of the sympathetic nerves or section of these nerves bring about, shows that these changes, interesting as they are, affect only peripheral conditions, and do not endanger life. But some of the post ganglionic fibres of the superior cervical ganglion enter the "brain" before they reach the periphery. May not some of these fibres also terminate in some vital point within the brain or the medulla? It is true, in our previous experimental studies, death of the animal was rather an exception. But these studies were essentially confined to the removal of a ganglion on one side only. From experiments upon the vagus nerves we know that cutting of one vagus does not affect the life of the otherwise normal animal, while, when both vagi are cut, with few exceptions, the animal dies within a day or two after the operation. May we not meet with a similar result by the removal of both ganglia? I therefore started a series of experiments in which both superior cervical ganglia were removed.

This series of experiments was made chiefly on rabbits. Although in these animals the superior cervical ganglion is small, it offers the advantage that it is not intimately connected with the vagus nerve, as it is the case in dogs and cats; the ganglion in rabbits may therefore be readily removed without causing injury to the neighboring vagus nerve. (It is not superfluous to state that the present series of experiments were carried out last winter, beginning November 3rd.) To this date more than eighty rabbits were used for the study of various phases of our problem. I shall state the results briefly.

For the chief issue of our problem we used twenty-eight animals in which both superior cervical ganglia were simultaneously removed under ether anesthesia. Of these, twenty-five died as follows: Six died in less than twenty-four hours, that is, the animal which was operated before noon or in the afternoon was found dead next morning at about nine o'clock. Nine animals died in less than two days, five in less than three days, one in four, one in five, one in six, one in eight and one in ten days. The autopsies revealed the presence of pulmonary lesions in all these animals. Three animals survived the removal of the ganglia and were killed after many weeks or months and no pulmonary lesions were found.

Both ganglia were also removed in two cats which died in less than two days and showed pulmonary lesions.

At an early stage of the investigation we met with one failure in a cat; it survived for many days the removal of both ganglia. Suspecting that the operation might not have been successful, it occurred to me, that this might be tested by the action of adrenalin upon the pupil. In the

experiments with adrenalin,[2] it was observed that when a ganglion was incompletely removed, instillation or subcutaneous injection of adrenalin did not cause the characteristic upon the pupil. I therefore applied this method to the surviving cat and found indeed that an instillation in a conjunctival sac as well as a subcutaneous injection of adrenalin neither caused a dilatation of the pupil nor a retraction of the nictitating membrane, the latter being one of the striking effects of adrenalin in ganglionectomized cats. The animal was then killed on the tenth day after the operation, and it was established that neither of the ganglia were successfully removed, and that the lungs showed no lesions. Also in one surviving rabbit it was found that adrenalin caused no dilatation of the pupil of the right eye. The autopsy showed normal lungs, proved that the ganglion on the right side was only partly removed. Henceforth an adrenalin test was made on the pupils of practically all animals in which the ganglia were removed. This was also done in the above mentioned three rabbits in which the removal of the ganglia did not lead to the death of the animals. In one of these animals the effect of adrenalin was indeed insignificant; in the other two rabbits, however, the instillation of adrenalin brought a definite dilatation of both pupils. In some rabbits the removal was purposely restricted to one half, or a little more than one half, of one ganglion or of both. As a rule the part to be removed was first crushed and then torn away. In these cases the adrenalin test was made a day or two later; the result was negative, and the animal survived even when both ganglia were mutilated.

However, in testing the success of the operation by the use of adrenalin, it has to be borne in mind that while a negative result prove that the corresponding ganglion was incompletely removed, a positive adrenalin test does not necessarily prove that the ganglia were so completely removed as to bring about the death of the animal. It may be that the number of nerve cells the removal of which is sufficient to bring about a positive adrenalin reaction upon the pupil, is smaller than the number of cells which have to be removed in order to bring about the death of an animal. In other words, the presence and integrity of a small number of nerve cells may be sufficient to maintain life, while the balance of the cells serve only as *factors of safety*—a condition which is especially met with in glands with internal secretion. It follows that in the above mentioned surviving rabbits in which the adrenalin test was positive, we had no assurance that the ganglia were so completely removed as to bring about the death of these animals. (It has to be added that at the autopsy of the three animals neither a minute macroscopical nor a microscopical search was made for possible remnants of the ganglia.)

However this may be, *this series of experiments showed that in about ninety per cent of the animals, the operative removal of both ganglia proved to be fatal to the animals—an experiment which, as far as I know, was never*

made before. The question now arose: Definite as the result is, is it important, that is, does it prove that the ganglia are really important to the maintenance of life, or was the fatal outcome perhaps due only to the operative procedure and not to the indispensability of some principle provided by the ganglia? Pulmonary lesions were found at the autopsy after the removal of both ganglia; pulmonary lesions are found after cutting both vagi. The ganglia are in the very proximity of the vagus nerves. May not the operative procedure injure both vagi sufficiently to bring about a "vagus pneumonia?"

The following considerations and experimental facts speak against such an interpretation. The possibility of injuring the vagus nerves was taken into consideration at the very beginning of this study. As it was stated before, it was just on account of this possibility that rabbits were given the preference. In these animals the superior cervical ganglion is separate from the vagus nerves, and it may be removed without touching the nerves or pulling at them. With this requirement in mind, I tried to carry out the experiment with care. It is not quite probable that I should have failed on both sides in nearly all my attempts, and that the injury which I might inadvertently have afflicted to both vagus nerves should have been of such an extent as to be equal in effect to a complete section of the nerves. Furthermore, in several experiments one of the ganglia could not be found and only one ganglion was removed. In these cases in which a long search for the ganglion was made the tissues and the corresponding vagus nerve had to be quite severely manipulated. The animals nevertheless survived this procedure. Finally in some experiments, the lower half of both ganglia were removed, as mentioned before. Here the lower half was first crushed and then removed, which required more manipulations than the tearing out of the entire ganglion. These animals survived the operation without manifesting any untoward symptoms.

More direct and decisive evidence was obtained by stimulations of the central end of the vagus nerves after removal of the corresponding ganglion, and after removal of both ganglia. The vagus nerves carry centripetal as well as centrifugal nerve fibres. The centripetal fibres affect and control the respiration and cause a change in the state of blood pressure. Further, the vagus trunk and the superior laryngeal nerve, a branch of the vagus, carry fibres the stimulation of which causes reflex deglutition. The vagus nerve seems to contain also sensory fibres. The stimulation was effected by Faradic currents of various strengths. The procedure was as follows: One vagus nerve was cut and the normal effect of stimulation established; then the corresponding ganglion was removed and the nerve again stimulated, and finally, the other ganglion was removed and the vagus stimulated. I shall state the results very briefly.

Respiration.—Stimulation of the vagus nerve after removal of the cor-

responding ganglion, or of both ganglia, gave results similar to those obtained before the removal, that is, active respiration, passive respiration (inhibition of the diaphragmatic movements), acceleration of the respiration, or a tetanic standstill of the diaphragm in an inspiratory state, according to the strength of the stimulus used and the individuality of the animal. *Bloodpressure.*—Stimulation of the vagus nerve gave a definite rise, and stimulation of the depressor nerve gave a fall. Rise and fall after removal of the ganglia were—at least— as good as before the removal. *Deglutition.*—When the animal was not too deeply narcotized, stimulation of the vagus trunk produced irregularly one deglutition or more, and stimulation of the central end of the superior laryngeal nerve produced regularly a series of swallows. *Sensation.*—Finally, it may be added that when the animal was nearly out of ether, stimulation with a strong current brought out signs of sensation, which gave the signal for an increase of the anesthesia. *These experiments show unmistakably that the afferent nerve fibres within the vagus were in no visible way affected by the act of removing the ganglia.*

The Centrifugal Fibres.—The efferent nerve fibres of the vagus, which concern us here, are those which innervate the muscles of the larynx, the pharyngeal muscles and the muscular fibres of the esophagus. The laryngeal innervation after removal of the ganglia has not yet been studied. However, clear evidence was obtained that the motor nerve fibres attending the pharynx and the esophagus were functioning in a normal way. *Under moderate anesthesia the inferior pharyngeal muscles were seen to contract with the rise of the larynx, which accompanies the initial stage of degutition, and the rise was followed by a normal peristaltic wave in the esophagus.*

The condition of the esophagus at the autopsy is another evidence that the vagus was not affected by the procedure of the removing of both ganglia. In the autopsies made on the twenty-five rabbits which died after the removal of both ganglia, the esophagus was found empty and contracted in fourteen cases; in the other cases the condition of the esophagus was not noted. In other words, in all the cases in which the esophagus was examined, it was found that after removal of the ganglia this tube was empty and contracted. On the other hand, in a series of eighteen rabbits in which both vagi were cut and in which nearly all animals died in less than twenty-four hours, at the autopsy the esophagus was found distended and filled with food in its entire length in thirteen animals; in the remaining five the esophagus was either only partly filled or entirely empty but was not exactly contracted. I wish to point out here that the upper part of the esophagus is partly innervated by pharyngeal nerves which remain intact when both vagi are cut in the neck. Moreover, food may be driven out by the rigor of the esophagus which, after the rigor passes away, may be relaxed again. At any rate, *it is a noteworthy fact that after the removal of the ganglia the esophagus was found*

empty and contracted in all cases in which the state of that tube was looked for, while in thirteen out of eighteen animals in which both vagi were cut, the entire esophagus was distended and full of food, a fact which speaks for the contention that the vagus nerves have not been affected by the removal of the ganglia.

From the foregoing evidences, I am inclined to conclude *that the death of the animals in which both ganglia were removed was due to the removal of these organs—if I may call them so—and not due to the procedure of the operation. In other words, the superior cervical ganglia contain a principle which is essential for the maintenance of life.*

As to the nature of the pulmonary lesions which were found after death following the removal of both ganglia, I shall only say that nearly in all instances there was a bronchopneumonia which was mostly located in the upper and middle lobes, and a pulmonary edema located mostly in the lower lobes of the lungs. In a few cases there were large and small abscesses in some parts of the lungs, and in some lungs there were plugs in the small bronchi which were apparently connected with the abscesses and which consisted of fibrin, pus and foreign material. In a few instances there were also serous or purulent pleurisies. I shall not attempt to enter into further details. Furthermore, I shall not discuss the question whether there is any difference between the pulmonary lesions observed after the removal of both ganglia and the lesions found in the lungs after section of both vagi. This I can the more afford to do, since the centuries' old question as to the nature of the pulmonary lesions after section of both vagi was recently opened up again by the important researches of Schafer[3]), and the entire question will surely have to be a subject of further investigations.

As to the nature of the mechanism by which the ganglia may control life, I shall, for the present, offer only a hypothesis. At the beginning of this communication, I called attention to the fibres from the superior cervical ganglia which enter the "brain," and put forward the question, whether some of these fibres may not terminate in a vital part of the medulla oblongata. The hypothesis answers this question in the affirmative, namely, that the fibres reach the respiratory centre in which they exert a controlling influence upon the coördinate antagonistic activities of the laryngeal muscles in the function of respiration. As we know, the glottis becomes wider during inspiration and narrower during expiration and is otherwise changing its configuration in the different respiratory phases. The larynx is provided with extrinsic and intrinsic muscles which act alternately as adductors and abductors and are innervated by different fibers running in the trunks of the laryngeal nerves. According to the law which I termed *Antagonistic Innervation* or the law of *Reciprocal Innervation* (Sherrington), the adductor muscles of the larynx become inhibited during the contraction of the abductors, and the latter become inhibited during

the contraction of the adductors. Such complicated continuous muscular activities suggest the control of a centre. This central control is maintained in a state of tonus. The hypothesis assumes that the tonus of the central laryngeal control is maintained by impulses coming continuously from the superior cervical ganglia. Some time after the removal of these ganglia the respiratory laryngeal centre loses its tonus and its coördinating activity upon the laryngeal muscles during respiration. The loss of coördination gives rise to results similar in some way to those consequent upon cutting of the vagus nerves. The difference between the two conditions is, that in cutting the vagus nerves, the *peripheral (motor) innervation of all the muscles* are simultaneously abolished, while after removal of the ganglia *only the central control* is eliminated. In this case impulses may still reach the laryngeal muscles from the respiratory centre, but they will now contract in an incoördinate and harmful manner. Future experiments may reveal that the behavior and appearance of the glottis after removal of the ganglia differ from its behavior and appearance after cutting of the vagi.

This supposed reflex action of the ganglia upon the control of the antagonistic contraction of the laryngeal muscles is somewhat parallel to the action of the same ganglia upon the peripheral organs, for instance, upon the iris. In this instance it controls the width of the pupil by causing either a contraction of the dilator muscle simultaneously with a relaxation of the sphincter pupilae, or, it causes a constriction of the sphincter with a simultaneous relaxation of the dilator.

As to the nature of the origin of the impulses, I compared above the ganglia with the glands of internal secretion. I append here a very brief report of a few experiments, the making of which was stimulated by the mentioned comparison. In four rabbits both superior cervical ganglia were torn away from their upper connections, but were left connected with the sympathetic nerves. In addition, two ganglia from another rabbit were placed deep in the wound before closing it. *All four animals survived many weeks* and were killed later by chloroform; the lungs were found normal. A fifth rabbit was killed six days after the operation in an experiment in which by accident only one foreign ganglion was added. At the autopsy a small abscess was found in the right middle lobe. Probably, the animal would have recovered. These few experiments do not permit any definite conclusion; but the findings are suggestive. If further experimentation should give similar results, the question would be obvious: *whether other sympathetic ganglia also possess some sort of an internal secretion.*

[1] Meltzer, S. J., and Auer, Clara Meltzer, "Studies on the Paradoxical Pupil-Dilatation Caused by Adrenalin. I.—The Effect of Subcutaneous Injections and Instillations of Adrenalin upon the Pupils of Rabbits," *Amer. J. Physiol.*, **11**, 1904 (28–36); Meltzer, S. J., "Studies on the Paradoxical Pupil-Dilatation Caused by Adrenalin.

II.—On the Influence of Subcutaneous Injections of Adrenalin upon the Eyes of Cats after Removal of Superior Cervical Ganglion," *Ibid.*, **11**, 1904 (37–39); Meltzer, S. J., and Auer, Clara Meltzer, "Studies on the Paradoxical Pupil-Dilatation Caused by Adrenalin. III.—A Discussion of the Nature of the Paradoxical Pupil-Dilatation Caused by Adrenalin."

[2] Meltzer, S. J. and Auer, Clara Meltzer, L. c. (30).

[3] Schafer, E. Sharpey, *Quart. J. Exper. Physiol.*, **12**, 1919 (231–301).

OBSERVATIONS ON THE BODY TEMPERATURE OF DRY COWS

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Communicated by H. P. Armsby, August 20, 1920

While a knowledge of the normal fluctuations in the body temperature of cattle is of importance to the veterinarian insofar as it may help to detect diseased conditions, it assumes special significance when metabolism experiments on cattle are made with the respiration calorimeter. By means of the latter, the heat eliminated by the animal during a certain period of time, as well as the gaseous exchange between the animal and the atmosphere that surrounds it, is measured. But in order to determine accurately the heat production as distinguished from the heat elimination a correction must be applied for any storage or loss of heat by the animal body and failure to do so might introduce an appreciable error. For example, if at the end of an experimental period the body temperature of an animal weighing 400 kilograms differs by 1° C. from that at the beginning, it means a storage or loss of heat by the body amounting to 332 calories (assuming the specific heat of the body to be 0.83). The data on record regarding the body temperature of farm animals are unsatisfactory for the reason that the observations have not been repeated often enough under different conditions which are known to affect the temperature of man. In this investigation an attempt has been made to secure data regarding the extent and the course of the body temperature variations in cattle and to study some of the factors that might influence them. The investigation covers a period of some sixteen weeks. The animals were two dry cows used at the same time for metabolism experiments with the respiration calorimeter, in which strict control of feeding, environment, etc., is maintained. Several series of observations on the body temperature of the cows have been made with special reference to the study of the following:

(1) Variations in body temperature from about 7.30 a. m. to about 5.30 p. m., including the effect of water drunk.

(2) Thermal gradient in the body.

(3) Variations in body temperature from about 5 p. m. to about 7 p. m., including the effect of the feed.